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(54) PROSTHETIC DEVICE

(71) We, W. L. GORE & ASSOCIATES, INC., a corporation organised and existing under the laws of the State of Delaware, U.S.A., of 555 Paper Mill Road, Newark, Delaware 19711, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to prosthetic devices, and in particular to artificial blood vessels.

The demand for replacements for human veins and arteries, especially those of small diameters, is high. The search hitherto for materials which could be used as arterial or venous replacements led to the use of solid-wall glass tubes, and thereafter to the use of various plastics materials and fabrics constructed from synthetic textile fibres.

In the early 1950's, advantages were found from the use of porous flexible plastics tubes rather than solid-walled tubes and a number of synthetic fibrous materials were woven or sewn into tubular configurations and used as porous arterial prostheses. Such materials performed satisfactorily for limited periods of time.

Over the past two decades, it has been proposed to use many different synthetic fibrous textile materials in various types of artificial vein and/or artery. Experiments in growing pigs, adult dogs, sheep, and to a more limited extent in man, have shown that the basic healing pattern in all animals is similar.

However, none of these hitherto proposed synthetic fibrous prosthetic devices has been entirely successful. Success requires an artificial arterial prosthesis to provide an open pathway for blood to pass along its entire length, and it should not generate embolisms to the distal arterial bed. All synthetic polymeric materials which have been proposed hitherto for the purpose exhibit varying degrees of surface thrombogenicity due to activation of plasma coagulation factors which lead to fibrin formation.

The following are the characteristics of an "ideal" vascular prosthesis, as defined by S. A. Weslowski and J. D. McMahon, (see "Artificial Arteries", AORN Journal, January, 1968):—

(1) absence of toxicity, allergenic potential or other overtly adverse chemical reaction; the biological reactivity of the material *per se*, over the range of that from Teflon (registered Trade Mark) to glass logical healing of the synthetic vascular prosthesis;

(2) the prosthesis should be durable without significant deterioration of the synthetic yarn upon prolonged implantation. Nylon (registered Trade Mark), Orlon (registered Trade Mark) and Ivalon (registered Trade Mark) are disqualified on this account; Dacron (registered Trade Mark), Vinyon-N (registered Trade Mark) and Teflon qualify. Dacron is preferable because of its superior mechanical handling properties during fabrication and at implantation;

(3) the biological heating porosity should be of the order of 10,000 millilitres of water/min./sq.cm. fabric at a pressure head of 120 mm Hg. It should be pointed out that no commercially available prosthesis today meets this specification because the limit of safe implantation from the viewpoint of hemorrhage is in the vicinity of 5000 ml. of water/min./sq.cm., at a pressure head of 120 mm. Hg;

(4) ideally, the material should have a low implant porosity to enable the administration of heparin or other anticoagulant: less than 50 cc min./cq.cm. at a pressure head or 120 mm. Hg; and

(5) there should be desirable handling properties which facilitate implanation which, therefore, becomes safer:

(a) conformability ("scrunchability") for ease of performance of anastomosis;

(b) linear elasticity is desirable; crimping in our experience is preferable to elastic yarn because with graft shortening the latter is more likely to affect adversely the porosity; and

(c) the fabrication should have good pliability and good twist characteristics for traversing flexion creases and subcutaneous

and subfascial tunnels without significant mechanical kinking.

According to the present invention there is provided a tube of expanded porous polytetrafluoroethylene capable of use as a vascular prosthesis and having a wall thickness of 20—62 mils, a density in the range of 0.22 to 0.34 g/cc and a microstructure consisting of nodes interconnected by fibrils, the length of the fibrils being not less than 5 microns.

By the word 'expanded' is meant stretched, and suitable methods for effecting such stretching are described in British Patent Specification 1,355,373.

The term 'microstructure' is used herein to refer to such structures which are of a size such that they cannot be resolved with the naked eye. The micostructure of nodes interconnected by fibrils can be as seen under 800× magnification. The length of the fibrils for a vascular prosthesis is preferably from 5 to 1000 microns.

Using a tubular prosthetic device in accordance with the invention as an artificial vascular replacement, tissue has been found to grow into and through the pores between the fibrils of the tube as healing proceeds. The result is a building scaffold or skeleton of polytetrafluoroethylene completely surrounded by and filled with new tissue. The spaces between the fibrils in the polymeric material before implantation may be very small, perhaps less than one micron. However, fibroblast cells appear to push aside the fibrils as they penetrate the porous structure of the polymer, and finally corpuscular blood circulation develops into and throughout the tissue that has invaded the fibrillar structure of the polymer. Thus, the open spaces between the fibrils, which may constitute 80 to 90% of the bulk volume of the device becomes completely filled with natural, living tissue. During the healing process, and without prior pre-clotting, such a tube-like device, which can be 80 to 90% porous, (the porosity being measured as the percentage ratio of the volume of said spaces to said bulk volume) can contain blood at arterial pressures. After healing, blood passage is through what is effectively a new-tissue tube, the blood then coming into contact with the inner surface (intima) of the tube which is of new tissue. Even prior to healing, this combination of synthetic-scaffold and new-tissue appears to be far less thrombogenic than hitherto proposed vascular replacements.

Devices in accordance with the invention are of expanded, porous polytetrafluoroethylene (hereinafter sometimes referred to as P.T.F.E.). Although for some applications comparatively low strength expanded polymers can be used, it is preferred that the polymer has a matrix tensile strength exceeding 7,300 psi in at least one direction. By definition, the tensile strength of a material is the maximum tensile stress, expressed in force per unit cross-sectional area of a specimen, which the specimen will withstand without breaking (see, for example, The American Society for Testing and Materials. "1970 Annual Book of ASTM Standards—part 24", page 41). The true cross-sectional area of solid material within a porous specimen is the cross-sectional area of the porous specimen multiplied by the fraction of solid material within that cross-section. This fraction is equivalent to the ratio of the apparent specific gravity of the porous specimen divided by the specific gravity of the solid material which makes up the porous specimen. Thus, to compute specimen, the maximum force required to break the sample is divided by the cross-sectional area of the porous sample, and multiplied by the ratio of the specific gravity of the solid material to the apparent specific gravity of the porous specimen. The matrix tensile strength is calculated by multiplying the tensile strength, computed as above, by the ratio of the specific gravity of the solid material to that of the porous specimen.

The microstructure of the polymer of prosthetic devices in accordance with the invention, as seen under 800X or greater magnification, consists of nodes interconnected by fibrils. A diagrammatic representation of this material, as it typically appears under microscopic examination, is shown in the accompanying drawing, in which the porous material 10 consists of nodes 11 interconnected by fibrils 12. The length of the fibrils 12 is not less than 5 microns. In tubular form, and when used as a vascular prosthetic device, the length of the fibrils 12 of the polymeric material will exceed 5 microns but it is preferably less than 1000 microns.

Devices in accordance with the invention can be manufactured by stretching suitably shaped, extruded, unsintered polytetrafluoroethylene, after removing liquid lubricants used in the conventional extrusion of the polymer (see British Patent Specification 1,355,373). The resulting expanded, porous polytetrafluoroethylene (PTFE) is strong, highly porous, flexible, conformable, and possesses the inert properties inherent to PTFE. It is chemically and biologically inert to almost all known substances, and before tissue invasion it possesses nearly all of the desirable properties of an "ideal" prosthetic material as hereinbefore defined. However, chemical and biological inertness are also possessed by woven Teflon (registered Trade Mark) and Dacron (registered Trade Mark) prostheses which have been used hitherto as artificial veins and arteries. However, after tissue has invaded prosthetic

devices in accordance with the invention, they function as a natural part of the body, which is entirely different from these hitherto proposed prosthetic devices.

Artificial vascular prosthetic devices made of porous, expanded PTFE give unexpectedly beneficial results, when the fibril length of the polymeric material is from 5 to 1000 microns. Within this range, and during healing, fibroblastic and capillary ingrowth into the prosthetic device occur, with uniform neointimal development over the devices and suture line surfaces.

Below about 5 micron fibril length, tissue ingrowth has not been found to occur. Above about 1000 micron fibril length, mechanical disadvantages can occur in suturing devices in the form of vascular grafts to the host blood vessel, and blood leakage can become a problem. The upper limit of fibril length is however, difficult to define quantitatively, since it depends to some extent upon the skill of the surgeon administering the graft. Blood leakage can also occur in vascular devices which have fibrils exceeding 1000 microns as a result of internal blood pressure. In the range of from 5 to 1000 micron fibril length, however, prosthetic devices in accordance with the invention can both contain the blood and simultaneously allow tissue ingrowth.

The preferred range of fibril length for artificial vascular prosthetic devices in accordance with the present invention is about 20 to 100 microns.

The internal diameter of tubular prosthetic devices in accordance with the invention is preferably less than 8 millimeters.

The following Examples are given by way of illustration only.

EXAMPLE 1

Two series of experiments were conducted in the dog, the two carotid arteries and the two femoral arteries being used as segmental replacement sites. In both series of experiments, all grafts were of expanded, porous PTFE tubes which were 4 cm. in length and 4 mm, in diameter. The wall thicknesses (20 to 32 mils), densities (0.25 to 0.34 g/cc), and fibril lengths (5 to 100 microns) were varied. No heparin was administered. Harvesting was effected at intervals from two weeks to four months after the grafts had been inserted. The sizes of the animals were selected to ensure a reasonable match between the natural blood vessel and the prosthetic graft. The results from the two series of experiments were as follows:—

The first series involved 64 implantations of which approximately 36 grafts were harvested and submitted for histological studies. The remaining grafts were in living animals with palpable pulses over the grafts. Eight of the harvested grafts were occluded, four of which were possibly due to technical errors in surgery recorded at the time of implantation. This provides an expected patency rate of 87.5% for the entire series. Histological examinations of patent grafts demonstrated fibroblastic ingrowth, capillary formation, and the development of uniform, smooth neointima throughout the lengths of the grafts, as well as over the suture line.

The second series of experiments involved the implantation of 107 grafts of which 51 were harvested at intervals ranging from two weeks to four months. Of these 51, 12 were occluded, yielding a 76.4% patency rate. The remaining 56 grafts were in living dogs with palpable pulses over the grafts, yielding an expected patency rate for the entire series of about 88%. In these two series, all grafts with a fibril length ranging from 5 to 20 microns yielded a 100% patency rate. Histological examination of all patent grafts showed transmural fibroblastic and capillary ingrowth with uniform neointimal development over the grafts and suture line surfaces.

EXAMPLE 2

Thirty-two grafts constructed from expanded, porous PTFE were substituted in one carotid artery in each of 32 sheep. The internal diameter of the grafts varied from 3 mm to 5.6 mm, with the graft lengths varying from 8 cm to 12 cm. The variables of wall thickness (20, 32, and 62 mils), density (0.22 to 0.34 g/cc), and fibril length (3 to 150 microns) were controlled. Heparin was administered during surgery. However, anticoagulants were not used during the post operative period. Grafts were harvested at intervals of three weeks, six weeks, three months, and six months. All these grafts were patent. The remaining grafts had palpable pulses over the grafts and were therefore patent.

Histological examination demonstrated that the grafts with fibril lengths ranging from 20 to 150 microns contained fibroblastic and capillary ingrowth as well as neointimal development throughout the lumen of the grafts. Grafts with less than 7 microns fibril length displayed an absence of fibroblastic and capillary ingrowth, with no neointimal development over the internal surface of the graft.

EXAMPLE 3

Grafts of expanded, porous PTFE tubes were interposed in the carotid artery, femoral artery, and femoral vein of mongrel dogs. The internal diameters of the grafts ranged from 2.8 mm to 3.3 mm, and all were 4 cm in length, and the wall thicknesses were 32 mils. The densities ranged from

0.21 to 0.35 g/cc and the fibril lengths ranged from 25 to 1000 microns. Of the 36 grafts implanted, 18 were harvested, three each at intervals of one month over a period of six months. Of these, none were occluded, yielding a 100% patency rate. Of the remaining 18 grafts, all were in living dogs with palpable pulses over the grafts, indicating patency. Therefore the expected patency rate for the entire series is 100%. Histological findings confirm both fibroblastic and capillary ingrowth with thin, uniform neointimal development.

EXAMPLE 4

In the past two decades a variety of prosthetic devices have been proposed for the replacement of large diameter arteries, e.g. over about 10 mm inside diameter. These prosthetic devices have failed to develop the neointima required for both long-term patency and the 100% elimination of microemboli (composed of platlet aggregates) which lead to neurological and physiological complications when they dislodge into the blood stream. Also, such hitherto proposed devices give poor results when utilized in the venous system where flow rates are extremely low.

In the present Example, 12 grafts of expanded, porous PTFE tube were interposed in the abdominal aortas of 12 dogs. All were 7.5 mm in diameter and 10 cm in length. All grafts had a wall thickness of 20 mils and fibril lengths of 20 to 40 microns. Of the 12 implants, five were harvested between three and six weeks and submitted for histological study. The remaining grafts were in living animals indicating patency. The five harvested grafts were patent with no presence of intimal thickening in any of the grafts. Histological examination of the five patent grafts demonstrated fibroblastic ingrowth and capillary formation. The expected patency rate for the experiment is 100%.

These results from animal research, where healing patterns are usually similar to those in man, clearly indicate the potential benefits to be achieved in human vascular replacement resulting from tissue ingrowth and capillary formation throughout the polymeric material of the devices, together with the absence of embolism-formation and a high degree of patency.

The fibril-node structure of the polymeric materials of prosthetic devices in accordance with the invention enables them to be used for other than vascular applications. Thus, tissue ingrowth has been shown to occur in skin grafts and in subcutaneously implanted membranes. Such grafts need not contain blood under the driving force of arterial pressure, and the upper limit of fibril length for such applications can then be greater than 1000 microns, it being limited only by mechanical considerations.

WHAT WE CLAIM IS:—

1. A tube of expanded porous polytetrafluoroethylene capable of use as a vascular prosthesis and having a wall thickness of 20—26 mils, a density in the range of 0.22 to 0.34 g/cc and a microstructure consisting of nodes interconnected by fibrils, the length of the fibrils being not less than 5 microns.
2. A tube according to claim 1 having a porosity of 80—90%.
3. A tube according to claim 1 or claim 2 wherein the polytetrafluoroethylene has a matrix tensile strength exceeding 7,300 p.s.i. in at least one direction.
4. A tube according to any preceding claim wherein the length of the fibrils is from 5 to 1000 microns long.
5. A tube according to any preceding claim wherein the length of the fibrils is from 20 to 100 microns long.
6. A tube according to any preceding claim wherein the internal diameter of the tube is less than 8 mm.
7. A tube according to claim 1, the tube being substantially as herein described in any of the Examples.

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1 SHEET *This drawing is a reproduction of the Original on a reduced scale*